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ABSTRACT

In the Federal Register of May 30, 1974, regulations were published as Part 46 of Title 45 of the Code of Federal Regulations providing generally for the protection of human subjects involved in research, development, or related activities supported by Department of Health, Education, and Welfare grants or contracts. This notice of proposed rulemaking is published to continue the public dialogue begun in November 1973, when the Director of the National Institutes of Health published draft proposals. These proposed rules cover minors, fetuses, abortuses, prisoners, and the institutionalized mentally disabled. (Author/JF)

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■

PROTECTION OF HUMAN SUBJECTS

Proposed Policy

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

[45 CFR Part 46]

PROTECTION OF HUMAN SUBJECTS

Proposed Policy

In the FEDERAL REGISTER of May 30, 1974 (39 FR 18914), regulations were published as Part 46 of Title 45 of the Code of Federal Regulations providing generally for the protection of human subjects involved in research, development, or related activities supported by Department grants or contracts. At that time it was indicated that notices of proposed rulemaking would be developed concerning minors, fetuses, abortuses, prisoners, and the institutionalized mentally disabled.

Coincidentally with the development of the notice of proposed rulemaking set forth below, both Houses of Congress reached agreement on the "National Research Act," and the President signed P.L. 93-348 into law. Among other things, the Act establishes an eleven-member National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research to "• • • (i) conduct a comprehensive investigation and study to identify the basic ethical principles which should underlie the conduct of biomedical and behavioral research involving human subjects, (ii) develop guidelines which should be followed in such research to assure that it is conducted in accordance with such principles, and (iii) make recommendations to the Secretary (I) for such administrative action as may be appropriate to apply such guidelines to biomedical and behavioral research conducted or supported under programs administered by the Secretary, and (II) concerning any other matter pertaining to the protection of human subjects of biomedical and behavioral research."

This notice of proposed rulemaking is published today to continue the public dialogue begun in November 1973 when the Director of the National Institutes of Health published draft proposals on these issues in the FEDERAL REGISTER. The comments addressed in this preamble are the result of that issuance.

The comments received as a result of this notice of proposed rulemaking will not only assist the Department to develop final regulations but will also be available to the Commission for their use during the course of their deliberations over the next two years.

In the light of the 450 responses received as a result of the November issuance, largely from grantee and contractor organizations, the Department now proposes that, in addition to the protection afforded generally to all subjects of research, development, and related activities supported by the Department by virtue of Part 46, further protective measures should be provided for those subjects of research whose capability of providing informed consent is or may be absent or limited.

This would be accomplished by amending Part 46 to delete § 46.19 through 46.22, redesignating § 46.1 through 46.18 as Subpart A, and adding new Subparts B through F. If this proposal is accepted, the regulations would be structured as follows:

Subpart A would be the basic regulation, substantially as promulgated on May 30, 1974. This provides that no activity involving any human subject at risk shall be supported by a DHEW grant or contract unless the applicant or offering organization has established an organizational review committee which has reviewed and approved such activity and submitted to DHEW a certification of such review and approval. This subpart also provides that all grant and contract proposals involving human subjects at risk are to be additionally evaluated by the Secretary for compliance with the requirements of said subpart.

Subpart B is reserved for a separate, future proposed rulemaking providing additional protection for children.

Subpart C as described in the present proposed rulemaking would call for the utilization of two special mechanisms for the protection of the pregnant woman and unborn child or fetus, where the pregnant woman participates in a research, development, or related activity. While these mechanisms are designed to allow sufficient flexibility for the pursuit of new information about the perinatal process, they are also designed to provide additional safeguards to assure that the research is acceptable from an ethical standpoint.

Subpart D as described in the present proposed rulemaking would give added responsibilities to an organizational review committee where the contemplated research would involve prisoners as subjects and also would require in such instances that a consent committee be established to supervise the selection and participation of prisoners in the research. Prisoner groups are particularly valuable in properly conducted clinical trials since they provide a stable subject population which can be followed over a period of weeks or months rather than days or hours. From the point of view of the prisoner subject, participation in research offers an opportunity to make a contribution to society and to provide an income, much as other jobs in prison do. Nevertheless, the dangers of abuse of prisoners' rights are obvious. For this reason, the proposed rulemaking calls for additional safeguards for the rights of prisoners whose capability to provide informed consent may be affected by the very fact of their incarceration.

Subpart E as described in the present proposed rulemaking offers additional protections for the rights of the mentally ill, the mentally retarded, the emotionally disturbed, and the senile who are confined to institutions, whether by voluntary or involuntary commitment. Such persons, by the very nature of their disabilities, may be severely limited in their capacity to provide informed consent to their participation in research. At the same time, the nature of their disabilities requires extensive research efforts to the study of the etiology, pathogenesis, and therapy of their conditions. The proposed rulemaking limits the research in which such subjects may be allowed to participate to that which is most likely to be of assistance to them or to persons similarly disabled.

In developing the present proposed rulemaking, the Department has taken into consideration the public's comments relevant to certain parts of the Introduction, Definition, and General Policy Sections of the draft regulations published at 39 FR 18914, November 16, 1973, as well as to the draft regulations themselves. The major comments, and the Department's present proposals, are as follows:

INTRODUCTION, GENERAL POLICY CONSIDERATIONS

A. Commentators suggested, in several different contexts, that the regulations should (i) apply to all research, regardless of the degree of risk or academic discipline concerned, and (ii) provide for the exclusion of certain types of research, particularly behavioral and social science research as distinguished from biomedical research.

The Department, having considered these comments, notes that the applicability provisions of the basic regulations (45 CFR 46.1) permit the Secretary to determine whether specific programs place subjects at risk. Such determinations are to be made only after careful study and publication in the FEDERAL REGISTER, providing an opportunity for comment on the merits of each determination. With respect to research in the social sciences, the Department has already indicated the intention of issuing public rulemaking on this matter (see 39 FR 18914, paragraph B).

B. Comments also included suggestions that regulations should be proposed specifically dealing with activities involving students, laboratory employees, terminally ill or terminal patients, the non-institutionalized mentally disabled, and other special groups.

The Department considers that any issues relating to these groups are less evident and that they are afforded the protections of the existing regulations published in 39 FR 18914.

C. Several comments suggested the promulgation of additional guidelines with respect to the distinction between established and accepted methods on the one hand and experimental procedures on the other.

While the Department recognizes the theoretical desirability of such guidelines, and that the practical necessity of making such a distinction is arising with increasing frequency, the feasibility of making this distinction on a generalized basis has yet to be demonstrated. At the present a regulatory approach to this issue does not appear justified.

D. It was suggested that all meetings of organizational review committees and similar groups established pursuant to

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these regulations should be open to the public.

The Department notes that since the purpose of these committees is, for the most part, to advise with respect to the conduct of individual projects and proposals by individual investigators, a blanket provision to this effect would appear to be inconsistent with the need to protect the confidentiality of the proceedings and records of institutional review and evaluation committees.

DEFINITIONS

A. Comments on the definition of "Subject at Risk" suggested changes in language that would (i) limit the concept of risk to that encountered only in addition to that normally experienced, (ii) eliminate demonstration projects as a possible source of risk, since these are nominally limited to application of established and accepted methods, (iii) specifically identify failure to maintain confidentiality as a source of risk, and (iv) provide a mechanism for identifying activities essentially free of risk.

These comments are similar to those made with respect to the same definition as incorporated in an earlier proposed rulemaking (38 FR 27882). In responding to the criticism, the Department has already (i) redefined "Subject at Risk" in 45 CFR 46.3(b) so as to exclude any activity which does not increase the ordinary risks of daily life or the recognized risks inherent in a chosen occupation or field of service, (ii) substituted in 45 CFR 46.1(a) the term "development" for "demonstration," (iii) provided in 45 CFR 46.19(b) specific prohibitions against disclosures of information which refers to or can be identified with a particular subject, and (iv) provided in 45 CFR 46.1(b) authority for determination in advance as to whether a particular Federal program or an investigational method or procedure may place subjects at risk.

B. Comments on the definition of "Clinical Research" suggested inclusion in said definition of the behavioral aspects of research and facets of medical research necessarily concerned with diagnosis and other nonetherapeutic aspects of research.

Since the term "clinical research" does not occur in the present rulemaking, the Department reserves its opinion with respect to these suggestions. However, the proposed regulations are applicable to all departmental research, development, and related activities except with respect to Subpart C, where applicability is limited to "biomedical research" (§ 46.303(b)).

C. Comments on "Informed Consent" suggested the addition of language concerning (i) full and complete disclosure, (ii) the likelihood of success or failure of the experiment, (iii) the use of placebos or other control procedures, (iv) provision of information as to the progress of the research, (v) publication of names of all persons, institutions, and review committees involved in approval of consent procedures, (vi) provision of legal counsel and technical advice, and (vii) assurance that the subject comprehends the disclosure.

The Department, having considered these comments, notes that "Informed Consent" is presently defined in 45 CFR 46.3(c) and not in the present proposed rulemaking. With respect to the specific suggestions the Department notes that: as far as (i) is concerned, the regulations already call for a "fair explanation" of the procedures and a description of risks and benefits reasonably to be expected; (ii) reflects a basic misunderstanding of the experimental process which begins, essentially, with the comparison of two or more methods, procedures, or modalities on the *a priori* hypothesis that there will be no difference; (iii) is implicit in the existing regulations and is better emphasized in interpretive materials; (iv) would not be an element of informed consent unless interim findings affected the risk of benefit involved; and (v) touches on the subject of a possible future proposed rulemaking and the Department reserves its options for the present. The suggestion in (vi) is met in part by the proposals in the present proposed rulemaking to employ consent committees to advise potential subjects. The last suggestion (vii) goes beyond requirements for informed consent as they have generally been articulated by the courts.

D. Comments also included suggestions for the inclusion of additional definitions of (i) Institutions, (ii) Legal Guardian, (iii) Organizational Review Committee, (iv) Institutionalized Mentally Infirm, and (v) Children (with regard to age of consent), Parents, and Father.

The Department, having reviewed these comments, notes that (i) "Organization" is defined for the purpose of these regulations to include "institutions" at 45 CFR 46.3(a); (ii) "Legally authorized representative" is defined for the purpose of these regualtions to include legal guardian at 45 CFR 46.3(h); (iii) the definition of "organizational review committee" is implicit in 45 CFR 46.6; (iv) "Institutionalized mentally disabled" has been defined in the present proposed rulemaking at 46.501(d) to meet the suggestion; and (v) definition of "Children," "Parents," and "Father" will be reconsidered prior to the issuance of a future rulemaking covering research on children.

E. Several commentators criticized provisions of the draft policy that would have required that activities to be conducted outside the United States satisfy all requirements of the Departments regulations including those based on ethical concepts peculiar to the Judeo-Christian moral heritage or to English common law. It was noted that this would create substantial problems for United States investigators working overseas since these concepts are often inconsistent if not in conflict with normal, ethical, and legal concepts in certain foreign countries. For the same reasons, it was argued that these provisions would create problems for United States citizens assigned, detailed, seconded, or acting as consultants to international organizations or to foreign governmental or private institutions.

Having considered these objections, the Department proposes to retain the basic concept that activities supported by Departmental funds should, in general, be subject to a uniform ethical policy wherever they are conducted, but to permit the Secretary to modify consent procedures if it can be demonstrated to his satisfaction that such procedures, as modified, are acceptable under the legal, social, and ethical standards of the locale in which the activities are to be performed.

FETUSES, ABORTUSES, AND PREGNANT WOMEN

Since comments on the draft provisions in 38 CFR 31738 providing additional protections for fetuses, abortuses, *in vitro* fertilization, and pregnant women were integrated with those on children, it is difficult to identify the communications specifically concerned with these subjects. However, it is estimated that the majority of the more than 400 letters received on research with children, born and unborn, touched on one or more aspects of research with fetuses, abortuses, and pregnant women.

A. A large number of respondents disagreed entirely with the idea of permitting research with the fetus, with the abortus (whether living or dead), or with the pregnant woman if the research might conceivably endanger the fetus.

The Department, having carefully considered these comments and similar proposals reflected in general correspondence and in articles in the public media, notes that their adoption would seriously hamper the development of needed improvements in the health care of the pregnant woman, the fetus, and the newborn. The opposition to research involvement of the fetus and abortus appears to be based in part on the assumption that the needed information can be obtained through research with animal species or with adults. Unfortunately, these assumptions are not valid. While much useful research can be conducted in animals, differences in species are nevertheless so great that any research finding in nonhuman species must ultimately be repeated in man before its general application in human medicine. In addition, the fetus and the newborn are not small adults. They suffer from some diseases not encountered in the adult. They may react differently to the diseases commonly affecting both adult and young, and they may have a different response to the same treatment, both with regard to its effectiveness and to its safety. The Department therefore proposes that (i) the ethical probity of any application or proposal for the support of any activity covered by subpart C be reviewed by an Ethical Advisory Board as described in § 46.304, and (ii) the conduct of any such activity supported by the Department be subject to oversight and monitoring by a consent committee as described in § 46.305.

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B. Opinion was divided as to the need for an Ethical Advisory Board. Many respondents called it a welcome addition in the review process. Others felt that it would duplicate the function of the local organizational review committee and that its existence would encourage the organizational review committee to be less critical and would impose an additional roadblock that would delay or prohibit important research while needlessly consuming time, energy, and money, and posing potential danger to a patient waiting for treatment. Complaints were voiced that such decisions should be made locally, not in Washington, and that the investigator should be able to present his case in person. Numerous comments suggested that the Board's function should be limited to advising on policy, guidelines, or procedures, and not be concerned with the review of individual projects. This would avoid duplicating the function of the organizational review committee. Others suggested that the Ethical Advisory Board should serve as an appeal body from the organizational review committee.

There were also numerous comments to the effect that it is unwise and impossible to totally separate ethical and scientific review. Approval based only on ethics would be unethical if the science were bad. Both should be reviewed jointly.

The Department, having reviewed these comments, concludes that Ethical Advisory Board remains, in concept, a useful addition to the review process. It does not duplicate the functions of the local organizational review committee, since the latter is primarily concerned with matters of organizational regulations, local standards of professional practice, applicable law within its jurisdiction, and local community attitudes. The Ethical Advisory Board will be primarily concerned with similar issues at the national level. Applications and proposals should be capable of passing scrutiny at both levels. It is therefore proposed that the Ethical Advisory Board be retained as part of the additional protection mechanism.

Specific comments regarding the establishment of an Ethical Advisory Board touched principally on (i) the possibility that appointment of members at an agency level might lead to "loaded" Boards, while appointment at a higher level, i.e., by a joint Congressional committee or by independent outside bodies, might produce a more objective group, and (ii) disagreement as to the proper balance between scientist and nonscientist members, with a majority of the commentators suggesting that more than one-third of the members should have the scientific expertise necessary to identify risks and their possible consequences. It was specifically suggested that different sizes, compositions, and administrative locations of the Board be tried before selecting a final mechanism. In addition, it was suggested (iii) that a fifteen member Board was too large, (iv) that all members be human geneticists, (v) that at least one member be a psychologist, if behavioral issues were to be considered, (vi) that there be an absolute ban on departmental agency employees, (vii) that all proceedings be confidential, (viii) that all meetings be open to the public, and (ix) that an appeal mechanism be established.

The Department, having considered these views, proposes that while an Ethical Advisory Board to deal with biomedical research involving fetuses, abortuses, pregnant women, and *in vitro* fertilization might logically be established at the National Institutes of Health, (i) the power of appointment should be reserved to the Secretary, (ii) while the membership should include research scientists, physicians, lawyers, clergy or ethicists, and representatives of the general public, the balance between callings should rest with the Secretary as should also (iii) the number of members, so that the membership (iv, v) can be adjusted to the needs of the Board as the workload and the issues before it dictate. The specific suggestion (see vi) that departmental agency employees be excluded is adopted and expanded to include all full-time employees of the Federal Government. The decisions with regard to suggestions (vii) and (viii) will be governed by the provisions of the Federal Advisory Committee Act which generally require that meetings of similar advisory groups be open to the public for the purposes of policy discussion, but closed and confidential for the purpose of review of specific applications and proposals. Since the Board will be advisory to funding agencies, the final action will be that of existing awarding authorities, and appeal mechanisms (ix) will be provided only to the extent available under other existing departmental regulations and policies. These proposals are incorporated into § 46.304.

C. A number of respondents recommended that the policy governing *in vitro* fertilization be strengthened, on the one hand, or liberalized, on the other. The Department has considered these recommendations, and has provisionally chosen not to stipulate at this time protections for the product of *in vitro* fertilization which is not implanted, but rather to leave that series of issues to the Ethical Advisory Board established under § 46.304(a). The Board will be required to weigh, with respect to specific research proposals, the state of the art, legal issues, community standards, and the availability of guidelines to govern each research situation.

Because biomedical research is not yet near the point of being able to maintain for a substantial period the nonimplanted product of *in vitro* fertilization, no clear and present danger arises from not stipulating in these regulations the protections for it. Given the state of the research, we believe that such stipulation would be premature.

It is the Department's intent that the definition of the term "fetus" (§ 46.303 (d)) be construed to encompass both the product of *in vivo* conception and the product of *in vitro* fertilization which is subsequently implanted in the donor of the ovum. Whatever the nature of the conception process, it is intended that upon implantation the protections of subpart C apply to all fetuses. It is only with respect to the protections available to the non-implanted product of *in vitro* fertilization that the regulations are silent.

With respect to the fertilization of human ova *in vitro*, it is expected that the Board will consider the extent to which current technology permits the continued development of such ova, as well as the legal and ethical issues surrounding the initiation and disposition of the products of such research.

With respect to implantation of fertilized human ova, it is expected that the Board will consider such factors as the safety of the technique (with respect to offspring) as demonstrated in animal studies, and clarification of the legal responsibilities of the donor and recipient parent(s) as well as the research personnel.

Since the Department does reserve the option of later specifying such protections by regulation, we invite comment on the question of appropriate regulations in the future.

D. The draft proposals included a suggestion for the establishment of a protection committee which elicited numerous comments that the use of the term "protection committee" implies that the Department recognizes a clear, present need for protection against the investigator, the uncertain relation of this committee to the organizational review committee, and the uniform need for and desirability for such protection.

Having reviewed these comments, the Department proposes an extensive revision in this innovative concept. Initially, it acknowledges that the term "protection committee" is pejorative and proposes the term "consent committee" as more appropriate and consistent with the primary purpose of such bodies. Further, it proposes to eliminate specific requirements for the size and composition of such committees. Instead, applicants and offerors are to propose the establishment of such a committee, specifying its size, composition, and rules of procedure. In addition, where the applicant or offeror believes that the activity involves only negligible risks, it may ask the Secretary to waive or modify the requirement for a consent committee. All proposals for the establishment, modification, or waiver of a consent committee shall be subject to review and approval at the local level by the organizational review committee and at the departmental level by the Ethical Advisory Board. The Ethical Advisory Board may prescribe additional duties for the consent committee. These changes are incorporated in § 46.305. In view of this drastic change in concept of the committee, detailed discussion of the many excellent and often thought-provoking comments concerned with details of the original draft seems inappropriate.

E. Many critical comments were addressed to the definitions used in this subpart, specifically:

1. "Pregnancy." It was suggested that pregnancy should be defined (i) conceptually to begin at the time of fertilization of the ovum, and (ii) operationally by actual test unless the woman has been surgically rendered incapable of pregnancy.

While the Department has no argument with the conceptual definition as proposed above, it sees no way of basing regulations on the concept. Rather, in order to provide an administerable policy, the definition must be based on existing medical technology which permits confirmation of pregnancy. This approach is reflected by § 46.303(c).

2. "Viability of the Fetus". Many recommendations were received concerning the definition of viability of the fetus after premature delivery or abortion. Some respondents urged that presence of fetal heartbeat be definitive (whether or not there is respiration) while others urged that identifiable cortical activity be specified as an alternative sign of viability. The Department has concluded that the issue of viability is a function of technological advance, and therefore must be decided with reference to the medical realities of the present time. We reserve the option of redefining the parameters as conditions warrant.

Only upon the basis of a definition which is both precise and consistent with current medical capability can a regulation realistically be interpreted and enforced. Current technology is such that a fetus, given the benefit of available medical therapy, cannot survive unless the lungs can be inflated so that respiration can take place. Without this capability, even if the heart is beating, the fetus is nonviable. In the future, if technology has advanced to the point of sustaining a fetus with non-inflatable lungs, the definition can and should be modified.

The Department has therefore chosen to specify, in the definition of viability of the fetus (§ 46.303(e)), that heart beat and respiration are, jointly, to be the indicator of viability.

3. "Abortus." Various comments noted that this definition is more restrictive than the usual medical definition of the abortus as a "nonviable fetus," and suggested substitution of the broader definition.

The Department proposes to retain the original definition for the purposes of these regulations. There is general agreement that there are distinct ethical problems involved in decisions concerning research use of the intact fetus, or use of organs or tissues obtained from a fetus that has died *in utero* or from an abortus at autopsy. The definition recurs with minor editorial changes in § 46.303(f).

F. Several comments were critical of the draft regulation's provisions limiting activities involving pregnant women to those not adversely affecting the fetus, except where the primary purpose of the activity was to benefit the fetus. It was suggested that the regulations (i) should contain language permitting exceptions for research necessary to meet the health needs of the mother, and (ii) should grant the right to participate in research aimed at improvement of methods of abortion, birth control, and genetic intervention.

The Department concurs with the first suggestion, (i), and proposes that the regulations permit research whose primary interest is to benefit the particular fetus or to respond to the health needs of the pregnant woman. It does not fully accept the second suggestion, (ii), and proposes that the regulations permit fetal research concerned with diagnosis and prevention of perinatal disease, and to offset the effects of genetic abnormality or congenital injury, but only when such research is done as part of a procedure properly performed to terminate a pregnancy. These changes are incorporated into § 46.306(a). The Department has tentatively concluded that consideration of risk vs. benefit with respect to fetal research does not seem to be appropriate.

G. Draft regulation provisions required maternal consent and the consent of the father if he were available and capable of participating in the consent process. This provision was strongly criticized on the grounds that it could permit the father of the fetus to deny needed health care to the woman or to the fetus even though he had no marital obligations, and that it might result in undue delay in the delivery of health care. It was also pointed out that the regulation did not touch on the question of the validity of consent by a pregnant minor.

The Department agrees. It is now proposed that paternal consent be sought only if the activity is not responding to the health needs of the pregnant woman and the father is reasonably available. These changes are reflected by § 46.306(b).

H. The Department has provisionally chosen, in § 46.306(a), to permit research to be undertaken from which there will be risk of harm to the fetus if such research is conducted as part of the abortion procedure. This decision, upon which we invite comment, has been made in the expectation that such research may produce new technology which will enable countless premature infants to live who now cannot.

It is not intended that this provision be construed to permit fetal research in anticipation of abortion prior to the commencement of the termination procedure itself.

While it is true that the class of fetuses for whom abortion is contemplated will be placed at greater research risk than all fetuses in general, such risk can arise only after implementation of the double safeguard of parental consent to the contemplated abortion, and second parental consent to the research procedure itself.

I. Comments regarding activities involving the abortus were concerned with the issue of maintaining vital functions and signs. It was argued that maintaining vital functions at the level of the organ, tissue, or cell is essential to studies and involves no prolongation of the dying of the abortus. At the same time, it was argued that termination of the heart beat should not be prohibited since temporary cardiac arrest has proved essential in the development of surgical techniques necessary to correct congenital heart defects.

Neither of these objections appear valid and no significant changes in § 46.307 are proposed. However, in order to emphasize again the distinction between research with the whole fetus or abortus, functioning as an organism with detectable vital signs, and with the dead fetus or abortus, the Department has added § 46.308, concerning activities involving a dead fetus or abortus, and § 46.309, concerning the abortus as an organ or tissue donor. Also § 46.307(d) has been expanded to permit the artificial maintenance of vital functions of an abortus where the purpose is to develop new methods for enabling the abortus to survive to the point of viability.

The Department feels that there is evident distinction between "termination" and "arrest" of the clinical signs as applied to the fetus or premature infant, but that no such distinction is valid or applicable where the abortus is concerned.

Prisoners

Forty-seven responses spoke to the provisions regarding additional protection for prisoners involved as subjects. Of these, two were from individuals identifying themselves as prisoners, seven were from State correctional institutions or State agencies, and four were from representatives of the pharmaceutical industry.

A. In comments directed at the overall nature of the draft regulations providing additional protection for prisoners, approximately equal numbers of respondents (i) denied that any significant additions were necessary, and (ii) proposed either the exclusion of prisoners from any research or experimentation not intended for the personal benefit of a prisoner, or highly restrictive regulations to accomplish the same purpose.

The Department, having reviewed these comments, has not been persuaded that any change should be made in the initial proposal.

B. A number of comments were concerned with the relationship between the existing organizational review committees and the proposed Protection Committee. It was pointed out by several that, as proposed, the two committees would not only have overlapping functions and authority but could operate independently of each other with conflicting directives and objectives that would not practicably provide additional protection of prisoners used as subjects.

The Department, recognizing the importance of preserving the authority of the organizational review committee as the primary institutional focus for the implementation of the Department of Health, Education, and Welfare regulations, proposes to assign to the organizational review committee the additional duties specified under § 46.404(a).

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A committee auxiliary to the organizational review committee, now designated the consent committee, will have the character and responsibilities specified in § 46.406. In keeping with this modified position it should be noted that when the organizational review committee determines that an activity would involve no risk or negligible risk to any prisoner while serving as a subject, the organization may request the Secretary to consider a modification or waiver of the requirement for a consent committee.

C. Comments on the proposed prohibition of research involvement of persons awaiting arraignment, trial, or sentencing expressed doubts that these individuals should be denied the benefits of innovative procedures, particularly those concerned with sociological research.

The Department agrees that the uniform exclusion of any such person from research should not be mandatory and proposes to permit his participation in an activity as a subject when the risk is negligible and the intent of the activity is therapeutic for him or relates to the nature of his confinement. This modification is incorporated into § 46.406.

D. The draft requirement for DHEW accreditation of prison facilities as sites for the performance of research, development, and related activities involving prisoner subjects was severely criticized, principally because of the jurisdictional problems inherent in any attempt to impose a Federal regulatory requirement on an autonomous State facility.

The Department concludes that this draft proposal was ill-advised. However, in order to attain the objective on an activity basis, certain specific prerequisities for the protection of prisoner subjects within facilities have been added to § 46.404(a) to properly relate conditions in a facility to the issue of undue inducements to participation by prisoners as subjects in an activity.

MENTALLY DISABLED

Over 40 of the responses spoke directly to the section of the draft concerned with the "mentally infirm." Many of these objected initially to the use of the word "infirm" as reflecting an antiquated notion of mental illness.

The Department agrees, and proposes to substitute "disabled" for "infirm," though noting that there is no clearly preferable collective term for the groups described.

A. Comments on the purpose of this section expressed satisfaction with the intent to provide additional protection for this group, but dissatisfaction with the actual language employed. Specifically, they noted that not institutionalization but rather the limitation of personal rights and freedom imposed by institutionalization is the determining issue. Similarly, it is not only the potential subject's difficulty in comprehending risks that is at issue, but his ability to comprehend generally.

The Department concurs. Proposed changes in language are incorporated in § 46.32.

B. Many of the respondents objected to one or more of the definitions peculiar to this subpart. The criticisms and the Department's proposed changes are as follows:

1. "Mentally infirm." In addition to requesting substitution of another term for "infirm," respondents raised conflicting objections to the definition's coverage. Some felt that it was overly inclusive; others felt it was too narrow. Some felt that epileptics should be specifically included, as well as those who are temporarily or permanently mentally incapacitated as a result of a physical condition such as stroke, brain damage, trauma, etc.

The Department, having carefully reviewed these comments, proposes no basic change in the definition. It concurs with many reviewers in the opinion that the definition is broad enough to include any category of subjects proposed for specific addition. Minor editorial changes have been made in § 46.503(b).

2. "Institutionalized." Commentators noted that (i) the regulations should cover all mentally disabled persons regardless of institutionalization, (ii) not all involuntary commitments are by order of a court, (iii) the draft refers to "residence" and "confinement" in similar contexts, though the terms do not carry the same connotation, and (iv) the definition does not specify halfway houses, lodges, day/night hospitals, nursing homes, and psychiatric wards of hospitals as places where subjects might be institutionalized.

The Department notes that (i) the non-institutionalized mentally disabled are covered by the existing regulations published as 39 FR 18914 and need not be included under these additional protections. Such individuals are not necessarily subject to all limitations on their freedom and rights as described in § 46.502 of this proposed rulemaking. Consideration will be given, however, to dealing with the noninstitutionalized legally incompetent who are mentally disabled in a subsequent notice of proposed rulemaking. With regard to (ii), the implication that court orders are the sole basis for involuntary confinement is incorrect and should be removed. Editorial changes have been made in § 46.503 to emphasize that concern therein is with those "• • • confined • • • in a residential institution • • •" (see iii) and, in order to designate the type of institutions concerned (see iv), it is proposed to separately define "Institutionalized mentally disabled individuals" in § 46.503 to include examples of such institutions. These changes are incorporated in § 46.503(c) and § 46.503(d).

C. While most respondents endorsed the intent of the draft limitations on activities involving the institutionalized mentally disabled, there were several specific criticisms of the terms used. Several persons suggested that any limitation of research to that related to a particular subject's "impairment" be worded so as to include any illness from which the person suffers so that, for example, an institutionalized mentally disabled person with cancer could not be denied the benefits of research in cancer therapy.

Further, this limitation could exclude the use of such subjects as controls in research which might benefit those suffering from a mental disability other than the specific one from which a particular subject suffers. Still further, mentally disabled people should be involved as subjects in research on infirmities other than their own because of lack of knowledge of the causes of mental and emotional disorders.

Many respondents felt that there was inadequate recognition of the need for research with the mentally disabled on basic psychological processes (e.g., learning, perception, and cognitive functions) which are fundamental to the study of the treatment, etiology, pathogenesis, prevention, and treatment of such disabilities.

The Department agrees that the language of the draft limiting research to the disease entities affecting individual subjects is probably not in the interests of the institutionalized mentally disabled as a class. The Department does not agree that it would be appropriate to permit this class of subjects to be involved in research unrelated to the causes, nature, or circumstances of their institutionalization. While there are possible disadvantages to the institutionalized mentally disabled in barring in this restriction, the possible risks of using the mentally disabled in such research outweigh its advantages. The proposed changes are incorporated in § 46.504(a). Editorial changes are reflected in § 46.504 (b) and § 46.504(c).

D. Criticisms of the draft's suggestion of the establishment or a protection committee in connection with such activity conducted in an institution for the mentally retarded were similar to those aimed at the protection committee to be established in connection with research on the pregnant woman and on the fetus. The Department proposes to change the title of the committee to "consent committee" and to change the regulations governing size, composition, and operating rules to conform to those previously described for § 46.505. Such changes are incorporated in § 46.505.

E. With respect to § 46.502(b), the Department reserves the right to amend this section if legislation now being developed by the Executive Branch on the safe guarding of individually linked data used for statistical and research purposes is enacted.

Written comments concerning the proposed regulation are invited from interested persons. Inquiries may be addressed and data, views, and arguments relating to the proposed regulations may be presented in writing, in triplicate, to the Chief, Institutional Relations Branch, Division of Research Grants, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20014. All comments received will be available for inspection at the National Institutes of

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Health, Room 303, Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland, weekdays (Federal holidays excepted) between the hours of 9:00 a.m. and 4:30 p.m. All relevant material received on or before November 21, 1974 will be considered.

Notice is also given that it is proposed to make any amendments that are adopted effective upon publication in the FEDERAL REGISTER.

Dated: August 15, 1974.

CASPAR W. WEINBERGER,
Secretary.

It is therefore proposed to amend Part 46 of Subtitle A of Title 45 of the Code of Federal Regulations by:

1. Revising §§ 46.19 through 46.22 and renumbering them as §§ 46.603 through 46.606, reading as set forth in Subpart F below.

2. Designating §§ 46.1 through 46.18 as Subpart A, renumbering these §§ 46.101 through 46.118, and modifying all references thereto accordingly.

3. Reserving Subpart B.

4. Adding the following new Subparts C through F.

Subpart C—Additional Protections Pertaining to Biomedical Research, Development, and Related Activities Involving Fetuses, Abortuses, Pregnant Women, and In Vitro Fertilization

Sec.
46.301 Applicability.
46.302 Purpose.
46.303 Definitions.
46.304 Ethical Advisory Board.
46.305 Establishment of a consent committee.
46.306 Activities involving fetuses *in utero* or pregnant women.
46.307 Activities involving abortuses.
46.308 Activities involving a dead fetus or abortus.
46.309 Activities involving the abortus as an organ or tissue donor.
46.310 Activities to be performed outside the United States.

Subpart D—Additional Protections Pertaining to Activities Involving Prisoners as Subjects

46.401 Applicability.
46.402 Purpose.
46.403 Definitions.
46.404 Additional duties of the organizational review committee where prisoners are involved.
46.405 Establishment of a consent committee.
46.406 Special restrictions.
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Subpart E—Additional Protections Pertaining to Activities Involving the Institutionalized Mentally Disabled as Subjects

46.501 Applicability.
46.502 Purpose.
46.503 Definitions.
46.504 Activities involving the institutionalized mentally disabled.
46.505 Additional duties of the organizational review committee where the institutionalized mentally disabled are involved.
46.506 Establishment of a consent committee.
46.507 Activities to be performed outside the United States.

Subpart F—General Provisions

46.601 Applicability.
46.602 Multiple consent committee requirements.
46.603 Organization's record; confidentiality.
46.604 Reports.
46.605 Early termination of awards; evaluation of subsequent applications.
46.606 Conditions.
46.607 Activities conducted by Department employees.

AUTHORITY: 5 U.S.C. 301.

Subpart C—Additional Protections Pertaining to Biomedical Research, Development, and Related Activities Involving Fetuses, Abortuses, Pregnant Women, and In Vitro Fertilization

§ 46.301 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting biomedical research, development, and related activities involving: (1) the fetus *in utero*, (2) the abortus, as that term is defined in § 46.303, (3) pregnant women, and (4) *in vitro* fertilization. In addition, these regulations are applicable to all such activities involving women who could become pregnant, except where the applicant or offeror shows to the satisfaction of the Secretary that adequate steps will be taken in the conduct of the activity to avoid involvement of women who are pregnant.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will in any way render inapplicable pertinent State or local laws bearing upon activities covered by this subpart.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 46.302 Purpose.

It is the purpose of this subpart to provide additional safeguards in reviewing activities to which this subpart is applicable to assure that they conform to appropriate ethical standards and relate to important societal needs.

§ 46.303 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Biomedical research, development, and related activities" means research, development, or related activities involving biological study (including but not limited to medical or surgical procedures, withdrawal or removal of body tissue or fluid, administration of chemical substances or input of energy, deviation from normal diet or hygiene, and manipulation or observation of bodily processes).

(c) "Pregnancy" encompasses the period of time from confirmation of implantation until delivery.

(d) "Fetus" means the product of conception from the time of implantation to the time of delivery.

(e) "Viability of the fetus" means the ability of the fetus, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. If the fetus has this ability, it is viable and therefore a premature infant.

(f) "Abortus" means a fetus when it is expelled whole, prior to viability, whether spontaneously or as a result of medical or surgical intervention. The term does not apply to the placenta: fetal material which is macerated at the time of expulsion; or cells, tissue, or organs excised from a dead fetus.

(g) "*In vitro* fertilization" means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor sperm and ova or by any other means.

§ 46.304 Ethical Advisory Board.

(a) All applications or proposals for the support of activities covered by this subpart shall be reviewed by an Ethical Advisory Board, established by the Secretary within the National Institutes of Health, which shall advise the funding agency concerning the acceptability of such activities from an ethical standpoint.

(b) Members of the Board shall be so selected that the Board will be competent to deal with medical, legal, social, and ethical issues and shall include, for example, research scientists, physicians, lawyers, and clergy and/or ethicists, as well as representatives of the general public. No Board member may be a regular, full-time employee of the Federal Government.

§ 46.305 Establishment of a consent committee.

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided an assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the Secretary) for each such activity, to oversee the actual process by which individual consents required by this subpart are secured, to monitor the progress of the activity and intervene as necessary, and to carry out such other duties as the Secretary (with the advice of the Ethical Advisory Board) may prescribe. The duties of the consent committee may include:

(1) Participation in the actual selection process and securing of consents to assure that all elements of a legally effective informed consent, as outlined in § 46.3, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of individual participation in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity. Depending on what may be prescribed in the application or offer approved by the Secretary, this might

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include: visits to the activity site, identification of one or more committee members who would be available for consultation with those involved in the consent procedure (i.e., participants) at the participant's request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the participants, periodic contact with the participants to ascertain whether they remain willing to continue in the activity, providing for the withdrawal of any participants who wish to do so, and authority to terminate participation of one or more participants with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (5) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of the members designated as chairperson.

(c) Where a particular activity, involving fetuses *in utero* or pregnant women, presents negligible risk to the fetus, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may (with the advice of the Ethical Advisory Board) grant the request in while or in part.

(d) The requirements of this section and § 46.304 do not obviate the need for review and approval of the application or offer by the organizational review committee, to the extent required under Subpart A of this part.

§ 46.306 Activities involving fetuses in utero or pregnant women.

(a) No activity to which this subpart is applicable, involving fetuses *in utero* or pregnant women, may be undertaken unless: (1) the purpose of the activity is to benefit the particular fetus or to respond to the health needs of the mother, or (2) the activity conducted as part of (but not prior to the commencment of) a procedure to terminate the pregnancy and is for the purpose of evaluating or improving methods of prenatal diagnosis, methods of prevention of premature birth, or methods of intervention to offset the effects of genetic abnormality or congenital injury.

(b) Activities covered by this subpart which are permissible under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their consent, except that the father's consent need not be secured if: (1) the purpose of the activity is to respond to the health needs of the mother or (2) his identity or whereabouts cannot reasonably be ascertained.

(c) Activities covered by this subpart which are permissible under paragraph (a) (2) of this section may not be undertaken unless individuals engaged in the research will have no part in: (1) any decisions as to the timing, method, or procedures used to terminate the pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy.

§ 46.307 Activities involving abortuses.

No activity to which this subpart is applicable, involving an abortus, may be undertaken unless:

(a) Appropriate studies on animals have been completed;

(b) The mother and father are legally competent and have given their consent, except that the father's consent need not be secured if his identity or whereabouts cannot reasonably be ascertained;

(c) Individuals engaged in the research will have no part in: (1) any decisions as to the timing, method, or procedures used to terminate the pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy;

(d) Vital functions of an abortus will not be artificially maintained except where the purpose of the activity is to develop new methods for enabling the abortus to survive to the point of viability; and

(e) Experimental procedures which would terminate the heart beat or respiration of the abortus will not be employed.

§ 46.308 Activities involving a dead fetus or abortus.

Activities involving a dead fetus or abortus shall be conducted in accordance with any applicable State or local laws governing autopsy.

§ 46.309 Activities involving the abortus as an organ or tissue donor.

Activities involving the abortus as an organ or tissue donor shall be conducted in accordance with any applicable State or local laws governing transplantation or anatomical gifts.

§ 46.310 Activities to be performed outside the United States.

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

Subpart D—Additional Protections Pertaining to Activities Involving Prisoners as Subjects

§ 46.401 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities involving prisoners as subjects.

(b) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 46.402 Purpose.

It is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable, inasmuch as, because of their incarceration, they may be under constraints which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate in such activities.

§ 46.403 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Prisoner" means any individual involuntarily confined in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute and also individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution.

§ 46.404 Additional duties of the organizational review committee where prisoners are involved.

(a) In addition to the responsibilities prescribed for such committees under Subpart A of this part, the applicant's or offeror's organizational review committee shall, with respect to activities covered by this subpart, carry out the following additional duties:

(1) Determine that there will be no undue inducements to participation by prisoners as subjects in the activity, taking into account such factors as whether the earnings, living conditions, medical care, quality of food, and amenities offered to participants in the activity would be better than those generally available to the prisoners;

(2) Determine that (i) all aspects of the activity would be appropriate for performance on nonprisoners, or (ii) the activity involves negligible risk to the subjects and is for the purpose of studying the effects of incarceration on such subjects;

(3) Determine that the application or proposal contains adequate procedures for selection of subjects, securing consents, monitoring continued subject participation, and assuring withdrawal with-

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out prejudice, in accordance with § 46.405 of this subpart;

(4) Determine that rates of remuneration are consistent with the anticipated duration of the activity, but not in excess of that paid for other employment generally available to inmates of the facility in question, and that withdrawal from the project for medical reasons will not result in loss of anticipated remuneration; and

(5) Carry out such other responsibilities as may be assigned by the Secretary.

(b) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an organizational review committee, subject to approval by the Secretary, where no such committee has been established under Subpart A of this part.

(c) No award may be issued until the applicant or offeror has certified to the Secretary that the organizational review committee has made the determinations required under paragraph (a) of this section.

§ 46.405 Establishment of a consent committee.

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided an assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the organizational review committee and the Secretary) for each such activity, to oversee the actual process by which individual subjects are selected and their consents secured, to monitor the progress of the activity (including visits to the activity site on a regular basis) and the continued willingness of the subjects to participate, to intervene on behalf of one or more subjects if conditions warrant, and to carry out such other duties as the Secretary may prescribe. The duties of the consent committee may include:

(1) Participation in the actual process by which individual subjects are selected and their consents secured to assure that all elements of a legally effective informed consent, as outlined in section 46.3 of this part, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of each individual's participation as a subject in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity and the continued willingness of subjects to participate. Depending on what may be prescribed in the application or offer approved by the Secretary, this might include: visits to the activity site, identification of one or more committee members who would be available for consultation with subjects at the subjects' request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the subjects, periodic contact with the subjects to ascertain whether they remain willing to continue in the study, providing for the withdrawal of any subjects who wish to do so, and authority to terminate participation of one or more subjects with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes a prisoner or a representative of an organization having as a primary concern protection of prisoners' interests; (5) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (6) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of its members designated as chairperson.

(c) Where a particular activity involves negligible risk to the subjects, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may grant the request in whole or in part.

§ 46.406 Special restrictions.

Persons detained in a correctional facility pending arraignment, trial, or sentencing or in a hospital facility for pre-arraignment, pre-trial, or pre-sentence diagnostic observation are excluded from participation in activities covered by this subpart, unless (a) the organizational review committee finds that the particular activity involves only negligible risk to the subjects and (b) the activity is therapeutic in intent or relates to the nature of their confinement.

§ 46.407 Activities to be performed outside the United States.

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

Subpart E—Additional Protections Pertaining to Activities Involving the Institutionalized Mentally Disabled as Subjects

§ 46.501 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities involving the institutionalized mentally disabled as subjects.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will necessarily result in a legally effective consent under applicable State or local law to a subject's participation in such an activity; nor in particular does it obviate the need for court approval of such participation where court approval is required under applicable State or local law in order to obtain a legally effective consent.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 46.502 Purpose.

It is the purpose of this subpart to provide additional safeguards for the protection of the institutionalized mentally disabled involved in activities to which this subpart is applicable, inasmuch as: (a) they are confined in an institutional setting where their freedom and rights are potentially subject to limitation; (b) they may be unable to comprehend sufficient information to give an informed consent, as that term is defined in § 46.103; and (c) they may be legally incompetent to consent to their participation in such activities.

§ 46.503 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Mentally disabled" includes those institutionalized individuals who are mentally ill, mentally retarded, emotionally disturbed, or senile, regardless of their legal status or basis of institutionalization.

(c) "Institutionalized" means confined, whether by voluntary admission or involuntary commitment, in a residential institution for the care or treatment of the mentally disabled.

(d) "Institutionalized mentally disabled individuals" includes but is not limited to patients in public or private mental hospitals, psychiatric patients in general hospitals, inpatients of community mental health centers, and mentally disabled individuals who reside in halfway houses or nursing homes.

§ 46.504 Activities involving the institutionalized mentally disabled.

Institutionalized mentally disabled individuals may not be included in an activity covered by this subpart unless:

(a) The proposed activity is related to the etiology, pathogenesis, prevention, diagnosis, or treatment of mental disability or the management, training, or rehabilitation of the mentally disabled and seeks information which cannot be obtained from subjects who are not institutionalized mentally disabled;

(b) The individual's legally effective informed consent to participation in the

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activity or, where the individual is legally incompetent, the informed consent of a representative with legal authority so to consent on behalf of the individual has been obtained; and

(c) The individual's assent to such participation has also been secured, when in the judgment of the consent committee he or she has sufficient mental capacity to understand what is proposed and to express an opinion as to his or her participation.

§ 46.505 Additional duties of the organizational review committee where the institutionalized mentally disabled are involved.

(a) In addition to the responsibilities prescribed for such committees under Subpart A of this part, the applicant's or offeror's organizational review committee shall, with respect to activities covered by this subpart, carry out the following additional duties:

(1) Determine that all aspects of the activity meet the requirements of § 46.50 (a) of this subpart;

(2) Determine that there will be no undue inducements to participation by individuals as subjects in the activity, taking into account such factors as whether the earnings, living conditions, medical care, quality of food, and amenities offered to participants in the activity would be better than those generally available to the mentally disabled at the institutions;

(3) Determine that the application or proposal contains adequate procedures for selection of subjects, securing consents, protecting confidentiality, and monitoring continued subject participation, in accordance with § 46.506 of this subpart; and

(4) Carry out such other responsibilities as may be assigned by the Secretary.

(b) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an organizational review committee, subject to approval by the Secretary, where no such committee has been established under Subpart A of this part.

(c) No award may be issued until the applicant or offeror has certified to the Secretary that the organizational review committee has made the determinations required under paragraph (a) of this section.

§ 46.506 Establishment of a consent committee.

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided a separate assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the organizational review committee and the secretary) for each such activity, to oversee the actual process by which individual subjects are selected and consents required by this subpart are secured, to monitor the progress of the activity (including visits to the activity site on a regular basis) and the continued willingness of the subjects to participate, to intervene on behalf of one or more subjects if conditions warrant, and to carry out such other duties as the Secretary may prescribe. The duties of the consent committee may include:

(1) Participation in the actual process by which individual subjects are selected and their consents secured to assure that all elements of a legally effective informed consent, as outlined in § 46.3, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of each individual's participation as a subject in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity and the continued willingness of subjects to participate. Depending on what may be prescribed in the application or offer approved by the Secretary, this might include: visits to the activity site, identification of one or more committee members who would be available for consultation with subjects at the subjects' request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the subjects, periodic contact with the subjects to ascertain whether they remain willing to continue in the study, providing for the withdrawal of any subjects who wish to do so, and authority to terminate participation of one or more subjects with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (5) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of its members designated as chairperson.

(c) Where a particular activity involves negligible risk to the subjects, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may grant the request in whole or in part.

§ 46.507 Activities to be performed outside the United States.

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

Subpart F—General Provisions

§ 46.601 Applicability.

Sections 46.602 through 46.606 are applicable to all grant or contract supported activities covered by this part.

§ 46.602 Multiple consent committee requirements.

Where an application or proposal would involve human subjects covered by more than one consent committee requirement imposed under this part, upon approval by the Secretary, these multiple requirements may be satisfied through use of a single consent committee appropriately constituted to take account of the nature of the subject group.

§ 46.603 Organization's records; confidentiality.

(a) Copies of all documents presented or required for initial and continuing review by the organization's review committee or consent committee, such as committee minutes, records or subjects' consent, transmittals on actions, instructions, and conditions resulting from committee deliberations addressed to the activity director, are to be retained by the organization, subject to the terms and conditions of grant and contract awards.

(b) Except as otherwise provided by law, information in the records or possession of an organization acquired in connection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) With the consent of the subject or his legally authorized representative; or

(2) As may be necessary for the Secretary to carry out his responsibilities under this part in the exercise of oversight for the protection of such subject or class of subjects.

§ 46.604 Reports.

Each organization with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

§ 46.605 Early termination of awards; evaluation of subsequent applications.

(a) If, in the judgment of the Secretary, an organization has failed materially to comply with the terms of this policy with respect to a particular Department of Health, Education, and Welfare grant or contract, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

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(b) In evaluating proposals or applications for support of activities covered by this part, the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) whether the offeror or applicant has been subject to a termination or suspension under paragraph (a) of this section, (2) whether the offeror or applicant or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects and (3) whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.606 Conditions.

The Secretary may with respect to any grant or contract or any class of grants or contracts impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

§ 46.607 Activities conducted by Department employees.

The regulations of this part (except for this subpart) are applicable as well to all research, development, and related activities conducted by employees of the Department of Health, Education and Welfare, except that: (a) subpart C is applicable only to biomedical research, development, and related activities and (b) each agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint.

[FR Doc.74-19000 Filed 8-20-74;8:45 am]

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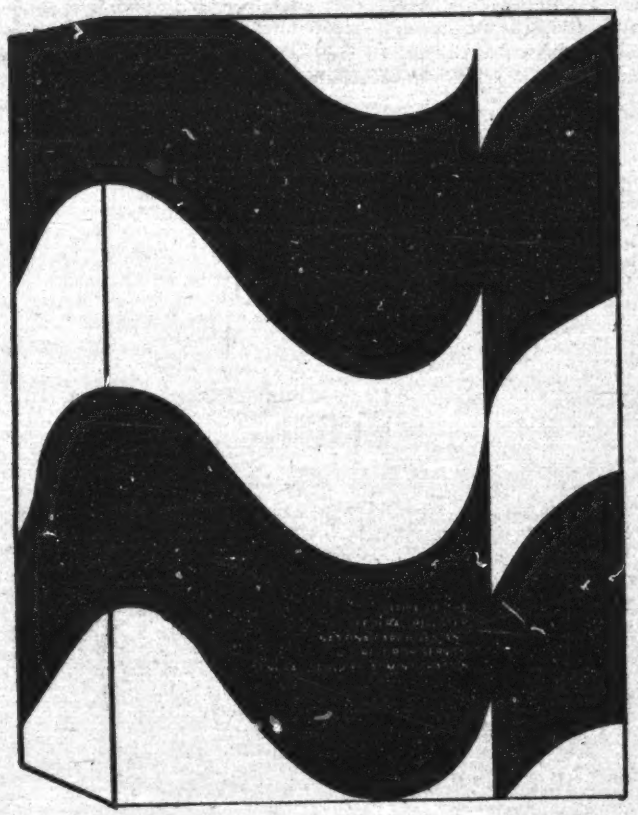
"Bureaucrat's Bible" or "Guerrilla Handbook"?



The Manual has been called the "bureaucrat's bible." It has also been called a "guerrilla warfare handbook for citizens tired of jousting with windmills."

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